

Variant: *NM_000527.5(LDLR):c.1444G>T (p.Asp482Tyr)*

Version: 1.0

CA10585455 [↗](#)

251845 (ClinVar) [↗](#)

Gene: LDLR ([HGNC:3949](#))

Condition: hypercholesterolemia, familial ([MONDO:0007750](#))

Inheritance Mode: Semidominant inheritance

UUID: c4be501c-7d06-4cc7-b16b-790eedd0fe3a

Approved on: 2023/6/23

Published on: 2024/9/25

HGVS expressions

NM_000527.5(LDLR):c.1444G>T (p.Asp482Tyr)

NM_000527.5:c.1444G>T

NC_000019.10:g.11113620G>T

CM000681.2:g.11113620G>T

NC_000019.9:g.11224296G>T

CM000681.1:g.11224296G>T

NC_000019.8:g.11085296G>T

NG_009060.1:g.29240G>T

ENST00000252444.10:c.1702G>T

ENST00000559340.2:c.1444G>T

ENST00000560467.2:c.1324G>T

ENST00000558518.6:c.1444G>T

ENST00000252444.9:c.1698G>T

ENST00000455727.6:c.940G>T

ENST00000535915.5:c.1321G>T

ENST00000545707.5:c.1063G>T

ENST00000557933.5:c.1444G>T

ENST00000558013.5:c.1444G>T

ENST00000558518.5:c.1444G>T

ENST00000559340.1:c.165G>T

ENST00000560467.1:c.924G>T

NM_000527.4:c.1444G>T

NM_001195798.1:c.1444G>T

NM_001195799.1:c.1321G>T

NM_001195800.1:c.940G>T

NM_001195803.1:c.1063G>T

NM_001195798.2:c.1444G>T

NM_001195799.2:c.1321G>T

NM_001195800.2:c.940G>T

NM_001195803.2:c.1063G>T

Uncertain Significance

Met criteria codes **3**

PP3

PM5

PM2

Not Met criteria codes **19**

Expert Panel

Familial Hypercholesterolemia VCEP [↗](#)

Criteria Specification Information **!**

PS1

PS2

PS3

PS4

BA1

PP1

PP4

PM1

PM3

PM4

PM6

BS1

BS4

BS3

BS2

BP4

BP3

BP2

PVS1

[Criteria Specifications for this VCEP](#)

Evidence Links 0

Evidence submitted by expert panel

Familial Hypercholesterolemia VCEP

The NM_000527.5(LDLR):c.1444G>T (p.Asp482Tyr) variant is classified as Uncertain significance - insufficient evidence for Familial Hypercholesterolemia by applying ACMG/AMP evidence codes PM2, PM5 and PP3 as defined by the ClinGen Familial Hypercholesterolemia Expert Panel LDLR-specific variant curation guidelines (specification version 1.2) on 23 June, 2023. PM2: This variant is absent from gnomAD (gnomAD v2.1.1). PP3: REVEL=0.99. PM5: 3 other missense variants in the same codon: - NM_000527.5(LDLR):c.1444G>A (p.Asp482Asn) (ClinVar ID 161284) - Pathogenic by these guidelines; - NM_000527.5(LDLR):c.1444G>C (p.Asp482His) (ClinVar ID 251844) - Likely Pathogenic by these guidelines; - NM_000527.5(LDLR):c.1445A>G (p.Asp482Gly) (ClinVar ID 251846) - Likely Pathogenic by these guidelines; There is 1 variant in the same codon classified as Pathogenic by these guidelines.

Met criteria codes

PP3			REVEL=0.99. It is above 0.75, so PP3 is met.
PM5			3 other missense variants in the same codon: - NM_000527.5(LDLR):c.1444G>A (p.Asp482Asn) (ClinVar ID 161284) - Pathogenic by these guidelines - NM_000527.5(LDLR):c.1444G>C (p.Asp482His) (ClinVar ID 251844) - Likely Pathogenic by these guidelines - NM_000527.5(LDLR):c.1445A>G (p.Asp482Gly) (ClinVar ID 251846) - Likely Pathogenic by these guidelines There is 1 variant in the same codon classified as Pathogenic by these guidelines. So, PM5 is met.
PM2			This variant is absent from gnomAD (gnomAD v2.1.1). So, PM2 is met.

Not Met criteria codes

PS1			No other missense variant in the same codon with the same amino acid change.
PS2			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS3			No evidence available.
PS4			No evidence available.
BA1			This variant is absent from gnomAD (gnomAD v2.1.1).

PP1			No evidence available.
PP4			No evidence available.
PM1			Not in exon 4. Not a cysteine residue.
PM3			No evidence available.
PM4			No in-frame deletions/insertions
PM6			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS1			This variant is absent from gnomAD (gnomAD v2.1.1).
BS4			No evidence available.
BS3			No evidence available.
BS2			No evidence available.
BP4			REVEL=0.99.
BP3			No in-frame deletions/insertions
BP2			No evidence available.
PVS1			Not a null variant

Curation History 		
   owing 1 to 1 of 1 rows		

The information on this website is not intended for direct diagnostic use or medical decision-making without review by a genetics professional. Individuals should not change their health behavior solely on the basis of information contained on this website. If you have questions about the information contained on this website, please see a health care professional.